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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

GITOMER, RALPH J

ART UNIT	PAPER NUMBER
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1623

DATE MAILED: 02/28/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/870,762

Applicant(s)

Fitzgerald et al.

Examiner

Ralph Gitomer

Art Unit

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on May 31, 2001.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-34 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

Priority is granted to 12/2/98. No PCT search report has been received. It would appear the present inventors may have made a number of presentations of the claimed invention with a different inventive entity. A complete IDS of all of the authors works is requested.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-23 are rejected under 35 U.S.C. 102(a or b) as being anticipated by Pratico.

Pratico (FASEB J) entitled "Increased F2-Isoprostanes in Alzheimer's Disease" teaches in the abstract, both iPF2a-III and iPF2a-VI measured by GC/MS is elevated in AD.

All the features in the claims are taught by Pratico for the same function as claimed.

Claims 1-5, 10-12 are rejected under 35 U.S.C. 102(a or b) as being anticipated by each of Morrow, Roberts, Mardini, Rokach, Pratico, Fitzgerald and Reilly.

5 Morrow (5,891,622) entitled ~~Assessment of Oxidative Stress in Vivo~~ with a 102(e) date of 2/1997, teaches in column 1 last paragraph, measurement of isoprostane concentrations correlate with free radical production and this measurement has significant diagnostic potential for assessment of oxidative stress. Free isoprostanes have been measured in plasma and urine as a relative
10 measure of oxidative stress in vivo. In column 4 first paragraph, the oxidative stress is determined through the comparison wherein the amount of isoprostanes is increased in the sample isolated from an organism undergoing oxidative stress compared to controls.

15 Roberts (5,700,654) entitled ~~Method and Compositions to Assess Oxidative Stress in Vivo~~ with a 102(e) date of 6/1991, teaches in column in column 3, oxidative stress is measured by measuring the amount of non-cyclooxygenase derived metabolites of prostanoids in a sample, comparing the measured amount of the
20 metabolites of prostanoids with a control and assessing the oxidative stress in vivo. In column 5 lines 15-20, prostaglandin F2 like compounds may also participate as mediators in the pathophysiology of oxidative stress and the compounds may be useful in the treatment of oxidative stress related diseases. In
25 column 7 assessing oxidant status in tissue by measuring the

level of prostaglandin F2 like compounds esterified to tissue phospholipids could be used to directly obtain evidence for the occurrence of free radical induced injury in the pathophysiology of a wide variety of human diseases. Mass spec can detect the quantity of prostaglandin F2 like compounds or their metabolites. The assay can be employed for measuring a variety of biological fluids.

Mardini (Circulation) with a different inventive entity than the present application, entitled ~~✖~~A Newly Discovered Isoprostane is a Marker of Oxidative Stress in LPS-Mediated Inflammation in Humans~~✖~~ teaches four families of isomers of prostaglandin F2 have been shown to be effective markers of oxidative stress and pathologic conditions.

Rokach (Recent Res Devel in Organic Chem) with a different inventive entity than the present application, entitled ~~✖~~Isoprostanes: Chemistry and Biological Significance~~✖~~ teaches on page 405 a significant development in the IP areas has been the identification of IPF2a-I in human urine using a synthetic standard and its deuterated derivative.

Pratico (Prostaglandins and Control of Vascular Smooth Muscle Cell Proliferation) entitled ~~✖~~Novel Indices of Oxidant Stress in Cardiovascular Disease: Specific Analysis of F2-Isoprostanes~~✖~~ teaches on page 27, the F2 series and 8-epi PGF2a in particulate are potential indices of oxidant stress in vivo. It is measured with GC/MS based selected ion monitoring assay

with a standard.

Fitzgerald (FASEB J) entitled ~~Isoprostanes~~: Indices of Oxidant Stress ~~teaches~~ in the abstract, 8-epi PGF2a is an index of oxidant stress.

5 Maxey (WO 94/04921) entitled ~~Isoprostane Protein Conjugates~~ teaches measuring isoprostanes in biological samples. On pages 1-2, a number of medical uses are discussed. On page 3 a number of isoprostanes are shown.

10 Reilly (Circulation) entitled ~~Increased Formation of Distinct F2 Isoprostanes in Hypercholesterolemia~~ teaches assays for specific isoprostanes including iPF2a-III, iPF2a-VI. It is noted that iPF2a-III is the same as 8-iso-PGF2a.

All the features of the present claims are taught by each of the above references for the same function as claimed.

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20 The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

25 (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered
5 therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103[®] and
10 potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 24-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pratico.

15 Pratico (FASEB J) entitled ~~✕~~Increased F2-Isoprostanes in Alzheimer's Disease~~✕~~ teaches in the abstract, both iPF2a-III and iPF2a-VI measured by GC/MS is elevated in AD.

Claims 24-32 differ from Pratico in that they are directed to treating disorders.

20 It would have been obvious to one of ordinary skill in the art at the time the invention was made to treat disorders diagnosed by determining isoprostanes because if the treatment were successful, one would expect the disease marker to change.

Claims 33-34 are directed to a kit.

One would be motivated to incorporate the claimed hardware and reagents into a kit with the expectation of commercial success because advantages include ease of automation, small volume of samples, faster analysis time, increased sensitivity and the potential for an increased degree of standardization. Controls are well known in this art and taught by the above references. Instructional material does not lend patentability.

Claims 24-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to identifying compounds for treating AD and their posology, treating disorders that raise the level of isoprostane markers, and kits.

The specification as originally filed does not provide written description of any compounds found for effectively treating AD nor their posology. Further, no other treatments for isoprostane elevating disorders are shown. And no kits are seen.

Claims 1-34 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Each of the following applies in all occurrences.

In claim 1 the level lacks antecedent basis. In claim 13(c) it is unclear what is intended. Claim 20 may be inconsistent regarding step (a) which includes a second mammal. In claim 25 the optimal lacks antecedent basis.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ralph Gitomer whose telephone number is (703) 308-0732. The examiner can normally be reached on Tuesday-Friday from 8:00 am - 5:00 pm. The examiner can also be reached on alternate Mondays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Geist can be reached on (703) 308-1701. The fax phone number for this Art Unit is (703) 308-4556. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1234. For 24 hour access to patent application information 7 days per week, or for filing applications electronically, please visit our website at www.uspto.gov and click on the button Patent Electronic Business Center for more information.

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